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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,751	07/02/2001	Wei Wang	DX0882XK	7429

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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 03/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/898,751	WANG ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,22,24-25,27-29,31 and 34-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,3,4,24,25 and 34-38* is/are allowed.

6)☒ Claim(s) *22,29 and 31* is/are rejected.

7)☒ Claim(s) *27 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Prosecution Application

The Request for Continued Examination (RCE) filed on 24 November 2003 under 37 CFR 1.114 based on parent Application No. 09/898,751 is acceptable and an RCE has been established. An action on the RCE follows.

Status of Application, Amendments and/or Claims

The amendment of 24 November 2003 has been entered in full. Claims 22 and 24 are amended. Claims 26, 30, and 32-33 are cancelled and claims 34-38 are added.

Claims 1, 3-4, 22, 24-25, 27-29, 31, and 34-38 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The rejection to claims 1, 3-4, and 24-25 under 35 U.S.C. § 112, first paragraph, as set forth at pg 2-6 of the previous Office Action (20 May 2003) is *withdrawn* in view of Applicant's persuasive arguments regarding intraperitoneal administration of anti-CTACK antibodies to mice in the specification (24 November 2003; pg 78, lines 23-30; pg 79, lines 1-2). It is noted that intraperitoneal injection of anti-CTACK antibodies resulted in significant suppression of skin inflammation on the ears of mice challenged with DNFB (pg 80, lines 9-24). In this case, intraperitoneal administration resulted in the antibodies being delivered to the ear systemically.

2. The rejection of claims 22, 27-29 and 31 under 35 U.S.C. § 112, first paragraph, as set forth at pg 6-10 of the previous Office Action (20 May 2003) is *withdrawn in part* in view of Applicant's persuasive arguments and submission of Kakinuma et al. (J Allergy Clin Immunol 111(3): 592-597, 2003). See 35 U.S.C. § 112, first paragraph, below.

Claim Objections

3. Claims 27-28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. Claims 22, 29, and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a patient suffering from allergic-contact dermatitis and psoriasis administering an effective amount of an antibody against cutaneous-T-cell attracting chemokine (CTACK), does not reasonably provide enablement for a method of treating a patient suffering from a skin disorder selected from the group consisting of wound healing and carcinoma comprising administering an effective amount of an antibody against cutaneous-T-cell-attracting chemokine (CTACK). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pg 6-8 of the Office Action of 29 November 2002 and at pg 6-10 of the Office Action of 20 May 2003.

Applicant's arguments (24 November 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that CTACK is specifically expressed in skin and selectively chemoattracts CLA+ skin-homing T cells (pg 70, lines 11-13). Applicant states that the CLA+ memory T cell subset constitutes a skin-associated population of memory cells that preferentially

extravasate at normal and chronically inflamed cutaneous sites. Applicant indicates that this subpopulation has been shown to be involved in local immunity and inflammatory cutaneous reactions (pg 69, lines 23-28). Applicant argues that distribution analysis in the specification (pg 65, line 5 through pg 68, line 24) show that CTACK RNA is expressed in human keratinocytes and upregulated by pro-inflammatory cytokines (pg 65, lines 29-30). Applicant contends that all the skin disorders claimed involve an inflammatory infiltration of cells from blood into skin. Applicant argues that these skin disorders, blocking the inflammatory infiltrate would be therapeutic as it would reduce inflammation associated with these disorders. Applicant submits that Appendix A contains publication abstracts that support a nexus between CTACK and allergic-contact dermatitis, psoriasis, wound healing, and carcinoma (Homey et al. Nat Med 8(2): 117-118, 2002; Szpaderska et al. J Dent Res 82(8): 621-626, 2003; Muller et al. Abstract for Invest Derm 2003 Meeting).

Applicant's arguments have been fully considered but are not found to be persuasive. The specification of the instant application does not teach treating a subject or patient suffering from wound healing or all possible carcinomas with anti-CTACK antibodies. Although the specification may suggest what skin disorders should be treated by CTACK or anti-CTACK antibodies (pg 10-11), this is not adequate guidance, but is merely an invitation for the artisan to use the current invention as a starting point for further experimentation. The specification does not disclose that CTACK is specifically involved in wound healing or in all carcinomas. For instance, although wound healing is an interactive process involving inflammation and infiltrating cells (Gillitzer et al. J Leukocyte Biol 69: 513-521, 2001; pg 513), the specification of the instant application does not indicate that CTACK is expressed or plays a role in wound

healing. A carcinoma is a malignant neoplasm derived from epithelial cells, which displays uncontrolled cellular proliferation and a tendency to invade adjacent tissues and to spread to distant sites by metastasis. Undue experimentation would be required of the skilled artisan to determine the role or expression of CTACK in the pathogenesis of wound healing and all carcinomas. Such information is necessary, especially in the determination of the optimal quantity, duration, and type of administration of anti-CTACK antibodies. One skilled in the art would not be able to predict from the allergen contact experiments of the instant specification that anti-CTACK antibodies would be able to treat the conditions/disorders of wound healing and all carcinomas.

Furthermore, Szpaderska et al. disclose that diminished inflammation is a key feature of the repair of oral mucosa wounds compared to skin wounds. However, Szpaderska et al. do not indicate that CTACK is expressed in oral mucosa wounds or skin wounds or that CTACK plays a role in wound healing.

Additionally, the Examiner acknowledges that Muller et al. discloses that the neutralization of CTACK (CCL27) results in delayed primary tumor growth of human melanoma cells in a SCID mouse model. However, Muller et al. delays the tumor growth of melanoma cells only, not all types of carcinoma (which is recited by the instant claims). Melanoma is a malignant neoplasm, derived from cells that are capable of forming melanin, arising most commonly in the skin of any part of the body, or in the eye. As mentioned above, a carcinoma is a type of cancer arising in epithelial tissue/cells (such as tissue lining internal or external organs or glandular tissue). The state of the art indicates that most human cancers are carcinomas (Tannock and Hill, The Basic Science of Oncology, New York: McGraw-Hill, 1998; pg 495). A

few examples of carcinomas include small cell lung carcinoma, renal cell carcinoma, squamous cell carcinoma, adenocarcinoma, etc. Undue experimentation would be required by the skilled artisan to treat all possible carcinomas by administration of an antibody against CTACK, as well as to determine the quantity, duration, and route of administration of the anti-CTACK antibody for each diverse type of carcinoma. Additionally, one skilled in the art would not be able to predict that the treatment of one carcinoma would be effective for another type of carcinoma. For example, Tannock and Hill teach that although objective and occasional complete responses to monoclonal antibodies recognizing surface determinants on cancer cells have been documented, the overall response rates and duration of responses has been disappointing (pg 430, 3rd full paragraph). Tannock and Hill disclose that a number of factors limit the therapeutic potential of monoclonal antibodies, such as tumor cell heterogeneity, antigenic cross-reactivity, antigenic modulation and shedding, and tumor penetration (pg 430-431).

(ii) Applicant also indicates that Appendix B contains data that provides additional evidence of a nexus between CTACK and a carcinoma as well as the therapeutic effect of an antibody against CTACK on a carcinoma *in vivo*. Applicant argues that CTACK was shown to induce migration and proliferation of melanoma cells. Applicant contends that blocking CTACK with an anti-mCCL27 (mCTACK) antibody was found to impair primary melanoma growth in mouse previously injected with tumor cells.

Applicant's arguments have been fully considered but are not found to be persuasive. Although Applicant indicates the graphs and diagram attached as Appendix B depict a nexus between CTACK and a carcinoma as well as the therapeutic effect of an antibody against

CTACK on a carcinoma *in vivo*, Applicant's argument is not persuasive because the evidence in the graphs must be submitted in the form of a declaration under 37 C.F.R. 1.132. An unsupported graph is not proper evidence, since it has not been peer-reviewed and its contents have not been attested to under 37 CFR 1.132. Without submission under 37 C.F.R. 1.132 , it is unclear where the data in the specification and the graphs originate from. However, if submitted under 37 C.F.R. 1.132, the results in Appendix B would still not be persuasive. Specifically, the graphs indicate that anti-CTACK (mCCL27) antibody blocks CTACK and impairs primary *melanoma* growth in a mouse previously injected with tumor cells as compared to isotype control (see B5). However, malignant melanoma is only type of carcinoma. A few examples of other carcinomas include small cell lung carcinoma, renal cell carcinoma, squamous cell carcinoma, adenocarcinoma, etc. The specification of the instant application and the results of Appendix B do not treat all types of carcinomas. Therefore, the undue experimentation would still be required by the skilled artisan to treat all possible carcinomas by administration of an antibody against CTACK. There is little or no guidance in the specification to determine the quantity, duration, and route of administration of an anti-CTACK antibody for each type of carcinoma. Additionally, one skilled in the art would not be able to predict that the treatment of one carcinoma would be effective for another type of carcinoma. The state of the art at the time the invention was made indicates the difficulties that are often encountered in the effort to use monoclonal antibodies as clinical reagents. See Tannock and Hill arguments, above.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to treat wound healing and all possible carcinomas with anti-CTACK antibodies, the lack of direction/guidance presented in the

specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of treatment of wound healing and all possible carcinomas, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

Claims 1, 3-4, 24-25, and 34-38 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
22 March 2004

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER